UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,666	06/28/2002	Markus Fandke	216087	6893

23460 7590 06/06/2005

LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6780

EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,666	FANDKE ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,50-56 and 64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,50-56 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is written in response to applicant's correspondence received 3/7/05. Claims 42 and 50-56 have been amended and claim 64 has been added. The remaining claims have been cancelled. Claims 42, 50-56, and 64 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Information Disclosure Statement

2. The newly submitted 1449 has been signed.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 42, 50-56, and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims 42 and 50-66 are drawn to methods for detecting L. brevis in a sample and require the use of nucleic acid molecules which hybridize with a region of L. brevis nucleic acid, wherein said nucleic acid molecules are (ii) a nucleic acid which specifically hybridizes

with a nucleic acid according a nucleic acid consisting of SEQ ID NO: 1, 21, 73, or 74, or a fragment of SEQ ID NO: 1, 21, 73, or 74, wherein the fragment comprises at least 10 nucleotides; (iii) a nucleic acid which is at least 70% identical with a nucleic acid according to a nucleic acid consisting of SEQ ID NO: 1, 21, 73, or 74, or a fragment of SEQ ID NO: 1, 21, 73, or 74, wherein the fragment comprises at least 10 nucleotides or (ii), and a nucleic acid which is complementary to a nucleic acid according to (ii) or (iii). Instant claim 64 differs from claim 42 because instant claim 64 requires that the nucleic acid molecules recited in part (iii) are at least 90% identical.

Dependent claims 50-56 claims do not further define the nucleotide sequence of the probes or primers.

Indeed, even for the rejected claims which recite SEQ ID NO, the recitations within these claims are sufficiently broad so as to encompass nucleic acid probes and primers to regions of the genome that are not disclosed in this application, and for which no written description of the many, many potential structures is provided.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only SEQ ID NO: 1, 21, 73 and 74 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

Claim Rejections - 35 USC § 102

5. Claims 42, 50, 53, 54, 55, and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Nietupski *et al.* (5484909).

Nietupski *et al.* teach methods for the detection of beer spoilage microorganisms of the genera Lactobacillus and Pediococcus. Nietupski *et al.* teach an embodiment wherein a segment of a target organism gene encoding Lactobicillus rRNA is amplified in a polymerase chain reaction (see example 3, Col. 23) and then the amplicon is detected via a hybridization probe. Nietupski et al. specifically teach the detection of L. brevis (Col. 24, lines 15-16).

Thus, Nietupski et al. teach a method for the detection of a microorganism relevant to brewing in a sample, which comprises the following steps:

(a) bringing the sample into contact with a combination of at least two first nucleic acid molecules (primers), which hybridize with a region of a microbial nucleic acid conserved in microorganisms relevant to brewing (a step which is inherent to PCR) ;

(b) amplification of the microbial nucleic acid or a portion thereof to produce at least one amplification fragment;

(c) bringing the amplification fragments obtained in step (b) into contact with at least one second nucleic acid molecule (probe), which specifically hybridizes with at least one amplification fragment that comprises a sequence of the microbial nucleic acid specific for all microorganisms relevant to brewing or for one or several families, genera, or species of microorganism relevant to brewing; and

(d) detection of at least one hybrid nucleic acid which consists of an amplification fragment and a second nucleic acid molecule introduced in step (c) whereupon a microorganism relevant to brewing is detected in a sample.

With regard to the sequence requirement in part (a) of claims 42 and 64, this claim broadly requires that the first nucleic acid molecules be nucleic acids which specifically hybridize with a fragment of SEQ ID NO: 1 that comprises at least 10 nucleotides. Thus, the claim encompasses any method which utilizes a nucleic acid molecule that would "specifically hybridize" to any fragment of 10 nucleotides from SEQ ID NO: 1. Nietupski *et al.* teach a number of such nucleic acid molecules for use in their methods, for example, SEQ ID NO: 9 taught by Nietupski *et al.* comprises nucleotides 12-19 of that sequence which are identical to nucleotides 202-209 of SEQ ID NO: 1. Thus, SEQ ID NO: 9 taught by Nietupski et al. would "specifically hybridize" to a fragment of nucleotides 200-209 of instant SEQ ID NO: 1, since the prior art nucleic acid molecule shares a common stretch of eight nucleotides with this ten nucleotide fragment. Likewise, SEQ ID NO: 10 taught by Nietupski *et al.* comprises nucleotides 14-21 of that sequence which are identical to the complement of nucleotides 194-201 of instant SEQ ID NO: 1. Thus, SEQ ID NO: 10 taught by Nietupski et al. would "specifically hybridize" to a fragment of nucleotides 192-201 of instant SEQ ID NO: 1, since the prior art nucleic acid molecule shares a common stretch of eight nucleotides with this ten nucleotide fragment. The instant claim language is quite broad in nature and encompasses the use of these nucleic acid molecules taught by Nietupski *et al.*as the first and second nucleic acids. Likewise, this analysis can be applied to the sequence requirements describing the probe of part (c). Further it is noted that the claim does not require that the nucleic acid molecule of part (c) have a

different sequence from one or both of the nucleic acid molecules of part (a), and thus, since Nietupski *et al.* teach amplification and detection using this pair of probes as primers and then sandwich detection using the same (see Col. 24, SEQ ID NO: 9 is probe 2891 and SEQ ID NO: 10 is probe 2892), thus the teachings of Nietupski *et al.* anticipate these claims.

With regard to claim 50, Nietupski *et al.* teach amplification with PCR.

With regard to claim 53, Nietupski *et al.* teach detection with probes that are modified to produce a detectable signal, the modification being a radioactive group (Col. 8, line 55).

With regard to claim 54 and 55, the nucleic acids taught by Nietupski *et al.* are at least 15 nucleotides long.

Thus, the teachings of Nietupski *et al.* anticipate the rejected claims.

6. Claims 42, 50, 53, 54, 55, and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 6-141899 (5/24/94) (referred to herein as "the Japanese reference").

A machine translation of the reference is provided with this office action for applicant's convenience.

The Japanese reference provides a method for the detection of L brevis in a sample. The method taught in the reference comprises the steps of bringing the sample into contact with at least two first nucleic acid molecules, amplifying the L. brevis nucleic acid to produce an amplification product, contacting the amplification fragments with at least one second nucleic acid molecule and detecting the amplification product as an indication of L. brevis in the sample. Thus, with regard to claims 42 and 64, the reference teaches a method for PCR amplification and subsequent detection of the PCR product of L. brevis nucleic acid in a sample using a PCR primer identified therein as SEQ ID NO: 1 (see ¶ 7, 12-18 and figure 1). This sequence has

100% identity with nucleotides 176-195 of instant SEQ ID NO: 1. The PCR method taught by the Japanese reference is within the scope of the instant claims. The instant claims recite the use of "at least two first nucleic acid molecules" and the PCR mix used in the Japanese reference would have many nucleic acid molecule copies of the primer SEQ ID NO: 1 in solution. Thus, the reference teaches bringing the sample into contact with "at least two" nucleic acid molecules that are a fragment of SEQ ID NO: 1 (that is, the claim does not require that the two molecules have different sequence). Likewise, with regard to part (c) of the rejected claims, the cyclic nature of the PCR reaction inherently means that amplification fragments are contacted with additional copies of the nucleic acid molecule in the PCR mix, which nucleic acid molecules are interpreted as meeting the limitation "contacting the amplification products obtained in step (b) with at least one second nucleic acid molecule." Again, there is no requirement that the second nucleic acid molecule be of different sequence than the first nucleic acid molecule.

With regard to claim 50, the amplification taught is PCR.

With regard to claim 53, the nucleotide sequences themselves are groups for immobilization onto a solid phase since these could be immobilized by hybridization to a capture probe. The claim does not require detection by this means, only that the second molecule contains "groups" for immobilization. A single nucleotide or a nucleotide sequence is such a group.

With regard to claims 54 and 55, SEQ ID NO: 1 taught in the reference is 20 nucleotides long.

Therefore, the teachings of the Japanese patent meet the limitations of the instant claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nietupski *et al.* in view of Backman *et al.*

Nietupski *et al.* teach methods for the detection of beer spoilage microorganisms of the genera Lactobacillus and Pediococcus. Nietupski *et al.* teach an embodiment wherein a segment of a target organism gene encoding Lactobicillus rRNA is amplified in a polymerase chain reaction (see example 3, Col. 23) and then the amplicon is detected via a hybridization probe.

Thus, Nietupski et al. teach a method for the detection of a microorganism relevant to brewing in a sample, which comprises the following steps:

(a) bringing the sample into contact with a combination of at least two first nucleic acid molecules (primers), which hybridize with a region of a microbial nucleic acid conserved in microorganisms relevant to brewing (a step which is inherent to PCR) ;

(b) amplification of the microbial nucleic acid or a portion thereof to produce at least one amplification fragment;

(c) bringing the amplification fragments obtained in step (b) into contact with at least one second nucleic acid molecule (probe), which specifically hybridizes with at least one amplification fragment that comprises a sequence of the microbial nucleic acid specific for all microorganisms relevant to brewing or for one or several families, genera, or species of microorganism relevant to brewing; and

(d) detection of at least one hybrid nucleic acid which consists of an amplification fragment and a second nucleic acid molecule introduced in step (c) whereupon a microorganism relevant to brewing is detected in a sample.

With regard to the sequence requirement in part (a) of claims 42 and 64, this claim broadly requires that the first nucleic acid molecules be nucleic acids which specifically hybridize with a fragment of SEQ ID NO: 1 that comprises at least 10 nucleotides. Thus, the claim encompasses any method which utilizes nucleic acid molecules that would "specifically hybridize" to any fragment of 10 nucleotides from SEQ ID NO: 1. Nietupski *et al.* teach a number of such nucleic acid molecules for use in their methods, for example, SEQ ID NO: 9 taught by Nietupski *et al.* comprises nucleotides 12-19 of that sequence which are identical to nucleotides 202-209 of SEQ ID NO: 1. Thus, SEQ ID NO: 9 taught by Nietupski et al. would "specifically hybridize" to a fragment of nucleotides 200-209 of instant SEQ ID NO: 1, since the

prior art nucleic acid molecule shares a common stretch of eight nucleotides with this ten nucleotide fragment. Likewise, SEQ ID NO: 10 taught by Nietupski *et al.* comprises nucleotides 14-21 of that sequence which are identical to the complement of nucleotides 194-201 of instant SEQ ID NO: 1. Thus, SEQ ID NO: 10 taught by Nietupski et al. would "specifically hybridize" to a fragment of nucleotides 192-201 of instant SEQ ID NO: 1, since the prior art nucleic acid molecule shares a common stretch of eight nucleotides with this ten nucleotide fragment. The instant claim language is quite broad in nature and encompasses the use of these nucleic acid molecules taught by Nietupski *et al.*as the first and second nucleic acids. Likewise, this analysis can be applied to the sequence requirements describing the probe of part (c). Further it is noted that the claim does not require that the nucleic acid molecule of part (c) have a different sequence from one or both of the nucleic acid molecules of part (a), and thus, since Nietupski *et al.* teach amplification and detection using this pair of probes as primers and then sandwich detection using the same (see Col. 24, SEQ ID NO: 9 is probe 2891 and SEQ ID NO: 10 is probe 2892), the methods taught by Nietupski et al. teach all of the elements of independent claim 42 from which the instantly rejected claim depends.

Nietupski *et al.* does not teach a method which utilizes a ligase chain reaction. However, at the time the invention was made, a variety of amplification techniques were known, one of which was the ligase chain reaction. Backman *et al.* teach improved methods of ligase chain reaction for amplification of nucleic acid templates.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have utilized the ligase chain reaction for the detection of microorganisms as taught by Nietupski *et al.* One would have been motivated to have modified

the methods taught by Nietupski *et al.* in order to provide an alternative method for the amplification of the target molecules.

10. Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nietupski *et al.* in view of Fraiser *et al.* (US 5744311).

Nietupski *et al.* teach methods for the detection of beer spoilage microorganisms of the genera Lactobacillus and Pediococcus. Nietupski *et al.* teach an embodiment wherein a segemtn of a target organism gene encoding Lactobicillus rRNA is amplified in a polymerase chain reaction (see example 3, Col. 23) and then the amplicon is detected via a hybridization probe.

Thus, Nietupski et al. teach a method for the detection of a microorganism relevant to brewing in a sample, which comprises the following steps:

(a) bringing the sample into contact with a combination of at least two first nucleic acid molecules (primers), which hybridize with a region of a microbial nucleic acid conserved in microorganisms relevant to brewing (a step which is inherent to PCR) ;

(b) amplification of the microbial nucleic acid or a portion thereof to produce at least one amplification fragment;

(c) bringing the amplification fragments obtained in step (b) into contact with at least one second nucleic acid molecule (probe), which specifically hybridizes with at least one amplification fragment that comprises a sequence of the microbial nucleic acid specific for all microorganisms relevant to brewing or for one or several families, genera, or species of microorganism relevant to brewing; and

(d) detection of at least one hybrid nucleic acid which consists of an amplification fragment and a second nucleic acid molecule introduced in step (c) whereupon a microorganism relevant to brewing is detected in a sample.

With regard to the sequence requirement in part (a) of claims 42 and 64, this claim broadly requires that the first nucleic acid molecules be nucleic acids which specifically hybridize with a fragment of SEQ ID NO: 1 that comprises at least 10 nucleotides. Thus, the claim encompasses any method which utilizes a nucleic acid molecule that would "specifically hybridize" to any fragment of 10 nucleotides from SEQ ID NO: 1. Nietupski *et al.* teach a number of such nucleic acid molecules for use in their methods, for example, SEQ ID NO: 9 taught by Nietupski *et al.* comprises nucleotides 12-19 of that sequence which are identical to nucleotides 202-209 of SEQ ID NO: 1. Thus, SEQ ID NO: 9 taught by Nietupski et al. would "specifically hybridize" to a fragment of nucleotides 200-209 of instant SEQ ID NO: 1, since the prior art nucleic acid molecule shares a common stretch of eight nucleotides with this ten nucleotide fragment. Likewise, SEQ ID NO: 10 taught by Nietupski *et al.* comprises nucleotides 14-21 of that sequence which are identical to the complement of nucleotides 194-201 of instant SEQ ID NO: 1. Thus, SEQ ID NO: 10 taught by Nietupski et al. would "specifically hybridize" to a fragment of nucleotides 192-201 of instant SEQ ID NO: 1, since the prior art nucleic acid molecule shares a common stretch of eight nucleotides with this ten nucleotide fragment. The instant claim language is quite broad in nature and encompasses the use of these nucleic acid molecules taught by Nietupski *et al.*as the first and second nucleic acids. Likewise, this analysis can be applied to the sequence requirements describing the probe of part (c). Further it is noted that the claim does not require that the nucleic acid molecule of part (c) have a

different sequence from one or both of the nucleic acid molecules of part (a), and thus, since Nietupski *et al.* teach amplification and detection using this pair of probes as primers and then sandwich detection using the same (see Col. 24, SEQ ID NO: 9 is probe 2891 and SEQ ID NO: 10 is probe 2892) the methods taught by Nietupski et al. teach all of the elements of independent claim 42 from which the instantly rejected claim depends.

Nietupski *et al.* does not teach a method which utilizes an isothermal amplification reaction. However, at the time the invention was made, a variety of amplification techniques were known, one of which was the ligase chain reaction. Fraiser *et al.* teach an isothermal stand displacement amplification reaction.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have utilized the isothermal stand displacement amplification reaction for the detection of microorganisms as taught by Nietupski *et al.* One would have been motivated to have modified the methods taught by Nietupski *et al.* in order to provide an alternative method for the amplification of the target molecules, and to take advantage of the SDA taught by Nietupski *et al.*, which Nietupski *et al.* teach has improved specificity, efficiency, reduced background amplification, and potentially improved yields (Abstract and throughout).

11. Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nietupski *et al.* in view of Fugono *et al.* (US 5738993).

Nietupski *et al.* teach methods for the detection of beer spoilage microorganisms of the genera Lactobacillus and Pediococcus. Nietupski *et al.* teach an embodiment wherein a segemtn of a target organism gene encoding Lactobicillus rRNA is amplified in a polymerase chain reaction (see example 3, Col. 23) and then the amplicon is detected via a hybridization probe.

Thus, Nietupski et al. teach a method for the detection of a microorganism relevant to brewing in a sample, which comprises the following steps:

(a) bringing the sample into contact with a combination of at least two first nucleic acid molecules (primers), which hybridize with a region of a microbial nucleic acid conserved in microorganisms relevant to brewing (a step which is inherent to PCR) ;

(b) amplification of the microbial nucleic acid or a portion thereof to produce at least one amplification fragment;

(c) bringing the amplification fragments obtained in step (b) into contact with at least one second nucleic acid molecule (probe), which specifically hybridizes with at least one amplification fragment that comprises a sequence of the microbial nucleic acid specific for all microorganisms relevant to brewing or for one or several families, genera, or species of microorganism relevant to brewing; and

(d) detection of at least one hybrid nucleic acid which consists of an amplification fragment and a second nucleic acid molecule introduced in step (c) whereupon a microorganism relevant to brewing is detected in a sample.

With regard to the sequence requirement in part (a) of claims 42 and 64, this claim broadly requires that the first nucleic acid molecules be nucleic acids which specifically hybridize with a fragment of SEQ ID NO: 1 that comprises at least 10 nucleotides. Thus, the claim encompasses any method which utilizes a nucleic acid molecule that would "specifically hybridize" to any fragment of 10 nucleotides from SEQ ID NO: 1. Nietupski *et al.* teach a number of such nucleic acid molecules for use in their methods, for example, SEQ ID NO: 9 taught by Nietupski *et al.* comprises nucleotides 12-19 of that sequence which are identical to

nucleotides 202-209 of SEQ ID NO: 1. Thus, SEQ ID NO: 9 taught by Nietupski et al. would "specifically hybridize" to a fragment of nucleotides 200-209 of instant SEQ ID NO: 1, since the prior art nucleic acid molecule shares a common stretch of eight nucleotides with this ten nucleotide fragment. Likewise, SEQ ID NO: 10 taught by Nietupski *et al.* comprises nucleotides 14-21 of that sequence which are identical to the complement of nucleotides 194-201 of instant SEQ ID NO: 1. Thus, SEQ ID NO: 10 taught by Nietupski et al. would "specifically hybridize" to a fragment of nucleotides 192-201 of instant SEQ ID NO: 1, since the prior art nucleic acid molecule shares a common stretch of eight nucleotides with this ten nucleotide fragment. The instant claim language is quite broad in nature and encompasses the use of these nucleic acid molecules taught by Nietupski *et al.*as the first and second nucleic acids. Likewise, this analysis can be applied to the sequence requirements describing the probe of part (c). Further it is noted that the claim does not require that the nucleic acid molecule of part (c) have a different sequence from one or both of the nucleic acid molecules of part (a), and thus, since Nietupski *et al.* teach amplification and detection using this pair of probes as primers and then sandwich detection using the same (see Col. 24, SEQ ID NO: 9 is probe 2891 and SEQ ID NO: 10 is probe 2892) the methods taught by Nietupski et al. teach all of the elements of independent claim 42 from which the instantly rejected claim depends.

Nietupski *et al.* do not teach a method which oligonucleotides that are modified in that up to 20% of the nucleotides in 10 consecutive nucleotides are replaced by nucleotides that do no naturally occur in bacteria. However, at the time the invention was made, it was routine to use modified nucleotides in oligonucleotide primers and probes. For example, Fugono *et al.* teach amplification primers which have the base inosine incorporated within the primer. Fugono *et al.*

teach methods which utilize primers wherein at least one base is replaced with inosine, and teach that the use of these alternative bases results in increased specificity (Col. 3).

Therefore, It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods taught by Nietupski *et al.* so as to have used modified bases as taught by Fugono *et al.* in order to have achieved the benefits of using such modified bases as taught by Fugono *et al.*

Response to Remarks

Written Description Rejection

The rejection for Written Description is applied to the amended claims and to the newly added claims. The rejection is modified to address the amended claims. The response traverses the rejection. Applicant points out that SEQ ID NO: 21, 73, and 74 are fragments of SEQ ID NO: 1 (response p. 8). This is not disputed. Applicant further states that that from the disclosure of these sequences, one would have recognized that the present application contemplates "fragments of SEQ ID NO: 1, 21, 73, and 74 comprising at least 10 nucleotides, as well as homologs and complements of SEQ ID NO: 1, 21, 73, and 74." The problematic aspect of the claims is as they relate to the portions of the claims which recite percent identity or molecules which "specifically hybridize" to the recited sequences. The scope of the molecules that are recited for use in the claims is quite broad considering the use of the language "specifically hybridizes" and the language "which is at least 70% identical" or "which is at least 90% identical" as recited in the claims. The claims encompass the use of, and therefore the detection of, a variety of molecules for which applicant has not provided written description, including, for

example, homologues and variants of the recited sequence. This includes potential sequences from closely related microorganism or strains of the L. brevis sequences provided in instant SEQ ID NO: 1, 21, 73 and 74. The specification teaches that instant SEQ ID NO: 1 is a sequence of the 23S-5S intergenic spacer of L. brevis (p. 198, ¶ beginning at line 9; and Table 1, p. 17). The specification teaches that instant SEQ ID NO: 21, 73, and 74 are "species-specific" molecules (p. 10 third ¶ beginning on the page; and Table 2), but the specification does not describe how any of these molecules can be modified even within 10% and certainly not up to 30% and still retain its species specificity, such as would be required for the practice of the instant invention. Further, the specification does not provide any definition for what it means to "specifically hybridize" and therefore this portion of the claim is broadly interpreted to include hybridization of fragments at any level of hybridization, since any hybridization that occurs would be a specific hybridization of the nucleotides with one another. The only written description of molecules which are species specific for L. brevis in the instant specification are those with SEQ ID NO: 1, 21, 73, and 74. For these reasons, the rejection is maintained.

Rejection under 102(b)

The rejection of claims 42, 50, 53, 54, 55, and 57 under 102(b) as being anticipated by Satokari et al. is WITHDRAWN because this reference does not teach or suggest the sequences required by the claims in part (a) and (c) of independent claim 42.

The rejection under Nietupski et al. has been modified to address the amended claims and newly set forth claim 64. Applicant argues that Nietupski et al. do not anticipate the claims because a BLAST comparison of SEQ ID NO: 9 and SEQ ID NO: 10 from Nietupski et al. revealed no sequence similarity between these sequences, and accordingly the patent does not

disclose nucleic acid molecules having at least 70% identity to any size fragment of SEQ ID NO: 1. This is not persuasive. Regardless of the results of the BLAST comparison conducted by applicants, the fact remains that the nucleotide fragments specifically pointed to in the rejection have identity with fragments within SEQ ID NO: 1 of the instant application. The rejection explains how the claims as broadly interpreted fairly encompass the methods taught by Nietupski et al. Therefore, the rejection is MAINTAINED.

An additional art rejection has been set forth to address the amended claims and the newly added claim 64.

Conclusion

12. Nucleic acids comprising instant SEQ ID NO: 1, 21, 73, and 74, each in their entirety are free of the prior art. Thus, methods which require any one of these are free of the prior art.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached by calling (571) 272-0745.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also

enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Examiner
Art Unit 1634

June 1, 2005